X-ray depilation of the scalp for fungous infection is almost a thing of the past since the introduction of griseofulvin.

Griseofulvin will not cure infections between the toes. Topical treatments are still the best alternative in such cases.

It is hoped that research will develop other antibiotics which may be of superior therapeutic value for superficial fungous infections and may also affect those due to deep fungi.

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SEPTIC SHOCK

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IN SPITE of the widespread use of antibiotics, death due to sepsis is still common in surgical patients.[1, 4] The purpose of this paper is to analyze the clinical, laboratory and postmortem data on 33 patients who died with a diagnosis of septic shock.

Endotoxin shock in dogs simulates many of the features of septic shock in humans. In order to investigate new avenues of therapy in septic shock, the endotoxin-shocked dog has been used as a convenient experimental model. Our observations on a new form of therapy carried out in the experimental animal are presented here.

CLINICAL MATERIAL

An analysis of the surgical deaths at the University of Alberta Hospital between January 1, 1956, and December 31, 1960, revealed that 33 patients died of septic shock. Twenty-six patients were male and seven were female. The eldest was 88 years of age and the youngest 18; the average age was 56.8 years. Shock was diagnosed when hypotension first became superimposed upon the infection. The duration of shock in one patient was 11 days; the shortest duration was 12 hours; the average was 4.6 days.

CLINICAL DATA

All patients showed evidence of an infective process. Thirty-two patients had a temperature of 99° F. or higher (Table I). The highest was 109° F.; the lowest 96.2° F.; the average 103° F. The patient in whom the temperature was 96.2° F. had a *Staphylococcus aureus* septicemia and hypotension. In five patients no bacteria were isolated on culture, but all five had hyperpyrexia and leukocytosis. The pulse rate was over 100 in 32 patients; the highest was 170 per minute; the lowest 90 per minute; the average 127. The average leukocyte count in 31 patients was 25,630 with high and low values of 47,800 and 2000 respectively. With the exception of one burned patient in whom it was impossible to record the blood pressure because of the burns, the systolic blood pressure was recorded in every case and prior to death had dropped to 90 mm. Hg or below. The average fall in systolic blood pressure from time of admission to onset of shock was 58 mm. Hg. The value of the CO_2 combining power in mEq./l. in one patient was as low as 4.5; the highest was 30.4 and the average 18.9, showing that acidosis was usually present. The blood urea nitrogen was usually elevated, the mean value being 56 mg. %.

TABLE I.—CLINICAL DATA ON 33 PATIENTS WITH SEPTIC SHOCK

	Maximum	*Minimum*	*Mean*
Age of patient (years)	88	18	56.8
Temperature (°F.)	109	96.2	103
Pulse rate	170	90	127
White blood cell count	47,800	2000	25,630
Hb. (g.%)	19.8	7.0	12.5
CO_2 (mEq./l.)	30.4	4.5	18.9
Blood urea nitrogen (mg. %)	200	8	56

PATHOLOGY AND BACTERIOLOGY

A postmortem examination was carried out in 25 patients. The conditions which were complicated by septic shock are recorded in Table II. Blood culture examinations were done in 17 patients of

TABLE II.—CONDITIONS COMPLICATED BY SEPTIC SHOCK

Condition	*Number*	*Per cent*
Peritonitis	15	45.5
Genitourinary instrumentation	6	18.2
Infected burns	3	9.1
Biliary surgery	3	9.1
Wound infection	2	6.0
Septic abortion	1	
Enterocolitis	1	
		12.1
Cardiac surgery	1	
Gastric surgery	1	

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TABLE III.—POSITIVE BLOOD CULTURES*

Organism	*Number*	*Per cent*
Staph. aureus	6	60
E. coli	2	20
Pr. vulgaris	1	10
Ps. aeruginosa	1	10
Total	10	100

*In 30.3% of patients.

which 10 were positive. Bacteria were isolated by culture from the infected area in 28 patients; and there was a mixed infection in three patients. Peritonitis was present in nearly 50% of the patients in this series in whom septic shock was a complication. This corresponds to the findings of Altemeier and Cole.[1] Genitourinary instrumentation was the next most common causative factor, while infected burns and biliary surgery comprised the majority of the remainder (Tables III and IV).

TABLE IV.—ORGANISMS CULTURED FROM FOCI OF INFECTION

Organisms isolated	*Number of patients*
E. coli	11
Staph. aureus	10
Ps. aeruginosa	3
Cl. welchii	2
Aer. aerogenes	2
Pr. vulgaris	1
Hemolytic streptococcus	1
Candida albicans	1
Total	31

DISCUSSION

The triad of a septic focus, hyperpyrexia and hypotension comprises the syndrome of septic shock. The presence of Gram-negative bacteria in the blood stream is frequently associated with the development of shock.[2] However, the production of shock by a Gram-positive bacteremia is not so well documented. The probable cause of shock complicating sepsis in man is an endotoxin liberated from the cell wall of dead bacteria. The endotoxin is a phosphorus-containing lipopolysaccharide-protein complex which can be isolated and purified by a variety of methods. In the experimental animal the intravenous injection of purified endotoxin produces a syndrome not unlike septic shock in man.

In the present series of cases, supportive therapy for hypotension in the form of noradrenaline or hydrocortisone was administered to 17 patients (51.5%). Noradrenaline was used alone or in conjunction with hydrocortisone in 10 patients, while hydrocortisone was given alone to the remaining seven patients; and 30 of the 33 patients received antibiotics.

Because the syndrome of septic shock is not well recognized, the diagnosis is often not made prior to death. The diagnosis should be considered when a surgical patient with a focus of infection and pyrexia develops hypotension. It is essential to take repeated blood cultures in these patients. A single negative blood culture is not sufficient to rule out the syndrome, while a positive culture will indicate an infection of such severity that the possibility of ensuing shock must be considered.

If the presence of this syndrome is suspected, a number of clinical and laboratory observations must be made: these will include frequent measurements of blood pressure and body temperature, blood cultures, serum electrolytes, pH and CO_2 estimations, urinary output studies, white cell counts and hematocrit measurements.

Intensive treatment directed at the source of infection must be instituted, with supportive treatment including the correction of fluid, electrolyte and pH imbalance; however, there is no standardized treatment for septic shock. Noradrenaline and hydrocortisone should be used, though the rationale for their use is not wholly understood. Because of the wide discrepancy in the methods of treatment in humans and the difficulty of assessing results of therapy in patients, we have attempted to study varying treatments in the endotoxin-shocked dog.

EXPERIMENTAL OBSERVATIONS

In the dog endotoxin is believed to cause shock by producing a widespread vasoconstriction in the smaller arterioles.[5] Among the disturbances in physiology which occur after the administration of this endotoxin are hemorrhagic necrosis of the bowel mucosa, loss of plasma, reduction in the circulatory blood volume, and diminished cardiac output. In order to correct the altered hemodynamics associated with a low cardiac output, a supplemental circulation consisting of an extracorporeal-pump-oxygenator was used at first. However, an assisted circulation alone did not save a great many of these animals from a fatal outcome. In order to reverse the widespread vasoconstriction, phenoxybenzamine hydrochloride (Dibenzyline),* a potent adrenergic blocking agent, was used in addition to the supplemental pump oxygenator. When Dibenzyline is given to dogs intravenously prior to the administration of endotoxin, it prevents death in some animals.[3] However, when given to dogs in established shock it does not influence the fatal outcome. Noradrenaline was not used, as it is known to potentiate endotoxin shock in the experimental animal.[3] The results which follow the use of the combination of Dibenzyline and an assisted circulation have proved to be encouraging.

METHOD

Endotoxin shock was produced in mongrel dogs by the intravenous injection of 5 mg./kg. of purified *E. coli* endotoxin; previous studies indicated that this dose was uniformly fatal. One hour after the injection of endotoxin, treatment was commenced. The blood pressure was monitored throughout by

*Kindly donated by Smith Kline & French Inter-American Corporation, Montreal, Quebec.

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cannulating a femoral artery and connecting it to a mercury manometer. Assisted circulation was provided by cannulating the femoral and jugular veins for the venous component of the system, and the other femoral artery for retrograde arterial perfusion. A sigmamotor pump and disposable plastic bag bubble oxygenator† comprised the pump-oxygenator unit.

Dibenzyline was given intravenously in a dose of 50 mg. diluted in 250 c.c. of glucose and saline. Perfusion was continued for 60 min., during which the Dibenzyline was infused slowly. Thirty-one dogs were used in the experiment and all were subjected to endotoxin shock: thirteen received no treatment and acted as controls; nine received assisted circulation alone; nine received assisted circulation and Dibenzyline.

RESULTS

In the control group all of the dogs died; the average length of survival was 16 hours. In the group receiving assisted circulation alone, the average length of survival was 23 hours, but all the dogs died. In the group receiving assisted circulation and Dibenzyline, the average length of survival in 6 dogs was 37 hours, while 3 were considered to be long-term survivors. All dogs that survived for 24 hours received intramuscular injections of penicillin and streptomycin, and intravenous infusions of glucose and saline. This routine was continued until the dogs died, or were well enough to eat (Table V).

†Pulmo-Pak, Abbott Laboratories.

TABLE V.—RESULTS OF TREATMENT IN EXPERIMENTAL ANIMALS

Number of dogs	*Groups*	*Average length of survival in hours*	*Survivors*
13	No treatment	16	0
9	Assisted circulation alone	23	0
9	Assisted circulation plus Dibenzyline	37	3

SUMMARY AND CONCLUSIONS

The clinical and laboratory data on 33 patients dying on the surgical services of the University of Alberta Hospital with a diagnosis of septic shock would indicate that the development of hypotension is an ominous sign in a patient with a septic focus who has an elevated body temperature.

Repeated blood cultures are essential in the clinical investigation. The existence of a positive culture should alert the clinician to the possibility of the complication of septic shock.

Endotoxin shock in dogs simulates many of the features of septic shock in humans; and the endotoxin-shocked dog is convenient for testing new methods of treatment.

A new form of therapy for endotoxin shock in dogs is described which has given encouraging results.

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PAGES OUT OF THE PAST: FROM THE JOURNAL OF FIFTY YEARS AGO

THE PREVENTION OF INSANITY

From the reports of the various Canadian institutions for the insane, I find that there were under treatment at the end of the last fiscal year of the several hospitals, upwards of 12,000 people who were being maintained at the public expense, at a cost, for the year, of nearly $2,000,000. These figures do not take into account those of our insane who are being maintained by private means, nor those who are under care at their homes, in county asylums, poor farms, and other places to which chronic, harmless patients are assigned. It would probably be quite safe to say that there are at least 25,000 insane people in Canada today. Of this number a large majority are not only useless members of society, being unable to earn anything or to contribute in any way to the general weal, but are actually costing the country fully $3,000,000 a year for their support.

Much attention is being given by students of sociology and economics, as well as by those directly associated with the care of the insane, to an apparent increase in the prevalence of insanity. That the number for whom institutional care is being sought is increasing in a much greater ratio than the general population, there can be no doubt. Much of this discrepancy, however, can be accounted for by such factors as the multiplication of institutions for the insane; the facility with which patients may now be transported to such institutions as compared with former times; an increased sensitiveness or intolerance of communities to those exhibiting mental warp; a decreased sense of responsibility on the part of relatives; possibly a lessened dread of asylums; and a growing tendency to voluntary entrance to these institutions. After due allowance is made for such factors, I believe that there is still reason to think that insanity is becoming more common. This is really what we should expect, for the general betterment of hygienic conditions, coupled with a decrease of alcoholism, and possibly also of tuberculosis, has placed restrictions upon nature's methods of eliminating the unfit, and doubtless permits the survival of many who would perish under such conditions as formerly prevailed. Of course, with further advance in preventive medicine, and especially as a result of effort directed particularly to the prevention of insanity, this seeming anomaly will disappear, but, meantime, the demand for institutional accommodation will, no doubt, continue to grow rapidly until practically all mental defectives are provided for.—W. H. Hattie, *Canad. M. A. J.*, 1: 1019, 1911.